0 (0–2), respectively. The median number of hospital admissions per patient was 1 (range 0–4). The reasons for acute care/ER visits and hospital admissions were tabulated below.

	Reasons for acute care/ER visits and hospital admissions
Acute care/ER visits	fever (n=23), bacteremia (2), dehydration (6), bronchiolitis (1), hemolysis (1), gastrointestinal bleeding (1), pseudotumor cerebri (2), bandemia (1)
Hospital admissions	conditioning (n=8), fever with no positive cultures (14), bacteremia (8), dehydration (4), bronchiolitis (1), hemolysis (1), gastrointestinal bleeding (1), pseudotumor cerebri (1), bandemia (1), CMV (1)

In 82.5% of hospital admissions (33/40), the clinical course was non-complex, with the discharge diagnosis the same as the admission diagnosis. In 17.5% (7/40), the course was complicated by conditions that developed while patients were in hospital, including bacteremia (n = 3), sepsis (3), adenovirus (1), respiratory distress (2), gastrointestinal bleeding (3), and organ failure (2). The median length of the non-complex and complex hospitalizations was 4 days (range 1–38) and 50 days (9–80), respectively. On any day, the mean probability that a patient would be an out-patient was 78.6% (CI 77.0–80.1%); the probability that the patient would be an in-patient for a non-complex or complex stay was 8.8% and 12.6%, respectively (CI 7.3–10.8% and 11.6–13.6%). In an earlier cohort, in which the busulfan AUC target was 4000–4600 microM-min (n = 17), 4 patients had primary graft failure and 3 died from related complications. In a later cohort with an AUC target of 5000 (n = 9), no patients had primary graft failure or death. Survival in these 2 cohorts was 81.2 and 100%, respectively (median follow-up 32.2 and 10.5 months). All engrafted patients have stable donor chimerism, improved lymphocyte counts, normalized immune function and decreased susceptibility to infection. Our data showed that ambulatory HSCT utilizing a RIC regimen was highly effective in children with PID.

67

IMPACT OF REDUCED INTENSITY CONDITIONING (RIC) IN PEDIATRIC ACUTE LYMPHOBLASTIC LEUKEMIA (ALL): A REPORT FROM THE CIBMTR

Verneris, M.R., Burke, M.J., He, W., Davies, S.M., Eapen, M., Wagner, J.E. CIBMTR, Milwaukee, WI

Significant experience now exists with reduced intensity condition (RIC) regimens prior to allogeneic hematopoietic cell transplantation (HCT) in adults with acute myeloid leukemia and non-ALL, lymphoid malignancies. Due to concerns that ALL may require more intensive therapy, there are few reports on the use of RIC, particularly in children with ALL. Therefore, we evaluated the transplant outcomes after RIC and allogeneic HCT in 41 children with ALL. In this retrospective analysis, all patients were aged 0–18 years with 64% aged 11–18 years; 44% had a Karnofsky score of <90%; and the disease status at the time of transplant was: 1st complete remission (CR) in 13%, 2nd CR in 41%, and >2nd CR in 26% and 21% had active disease. The time from diagnosis to transplant for 1st CR patients was 9 months (8–62 months) and for ≥2nd CR patients it was 32 months after 1st CR (range, 6–89 months). 63% were transplanted after 2000. A TBI-based conditioning regimen was used in 33% of patients, while the remainder (66%) received non-TBI containing regimens consisting of: busulfan (34%), cyclophosphamide (15%) and melphalan (17%). Matched related donors, were available for 37% (50% BM and 50% PBSC), with the remaining (63%) having unrelated donors (BM in 19%, PBSC in 55% and cord blood in 23%). Most had GVHD prophylaxis with a calcineurin inhibitor in combination with either methotrexate (47%) or other agents (41%). The disease free survival (DFS) and overall survival (OS) at 3 yrs was 31% (95% CI, 16–47%) and 38% (95% CI, 22–54%), respectively. Transplant related mortality (TRM) at 100 days and 3 years was 18% (95% confidence interval (CI, 7–30%) and 30% (95% CI, 16–46%). The incidence of aGVHD (Grade II-IV) at day +100 was 35%. At 3 years, cGHVD developed in 23% of patients. Relapse at 3 years was 39% (95% CI, 23–57). This is the largest series describing outcomes in pediatric patients with ALL undergoing allogeneic HCT after a RIC. While additional analyses are required, these data demonstrate that long term DFS and OS can be achieved using RIC regimens in pediatric patients with ALL.

SOLID TUMORS

68

ADOPTIVE TRANSFER OF HER2-SPECIFIC T CELLS ERADICATES EXPERIMENTAL GLIOBLASTOMA MULTIFORME

Salsman, V.S.[1], Kew, Y.[2], Powell, S.Z.[2], Wels, W.E.[3], Grossman, R.[2], Heslop, H.E.[1,2], Gottschalk, S.[1], Ahmed, N.[1] [1] Baylor College of Medicine, Houston, TX; [2] Weil-Cornell Medical College, Houston, TX; [3] Georg-Speyer-Haus, Frankfurt Am Main, Germany

Background: The intent of this project is to develop an effective adoptive immunotherapy for glioblastoma multiforme (GBM), which remains largely incurable with current treatment disciplines. New therapies are thus needed to improve current outcomes without increasing treatment-related morbidities. Immunotherapies have the potential to fulfill this need, since they are highly tumor-specific and cause minimal bystander cell damage. We propose to use T cells to target the human epidermal growth factor receptor 2 (HER2), a surface antigen, which is overexpressed in GBM. While the use of HER2 monoclonal antibodies has been limited by low levels of HER2 expression on GBMs, we show here that T cells expressing HER2-specific chimeric antigen receptors (CAR) have potent anti-tumor activity both ex vivo and in animal models.

Methods: T cells from GBM patients were retroviraly transduced to express HER2-specific CAR with a CD28.ζ signaling domain (HER2-specific T cells). Primary GBM cells and GBM cell lines were used to test the function of the generated HER2-specific T cells. The ex vivo efficacy was determined by their ability 1) to kill HER2-positive target cells in a cytoxicity assay and 2) to proliferate and secrete cytokines (IFN-γ and IL-2) in response to stimulation with HER2-positive tumor cells. The in vivo efficacy of the HER2-specific T cells was tested for the ability to induce tumor regression in an orthotopic murine xenograft model.

Results: Primary HER2-specific T cells killed both HER2-positive autologous GBM cells and GBM cell lines in cytotoxicity assays, whereas HER2-negative targets were not killed. Stimulation of HER2-specific T cells with HER2-positive primary GBM cells and GBM cell lines resulted in T-cell proliferation and secretion of IFN-γ and IL-2 in a HER2-dependent manner. Intra-tumoral injection of HER2-specific T cells resulted in eradication of established GBM xenografts in an orthotopic murine model. In contrast, delivery of non-transduced T cells did not change the tumor growth pattern.

Conclusion: We demonstrate that T-cells expressing HER2-specific CARs can recognize and kill HER2-positive GBMs. Their activation results in proliferation and secretion of immunostiumlatory cytokines. HER2-specific T cells can effectively eradicate established GBM xenografts in an orthotopic murine model. These results indicate that HER2-specific T cells could represent a promising immunotherapeutic approach for GBM.

STEM CELL BIOLOGY

69

IDENTIFICATION AND ISOLATION OF THE HEMATOPOIETIC STEM CELL NICHE INITIATING CELL POPULATION

Kraft, D., Chan, C., Chen, C.-C., Luppen, C., Weissman, I.L. Stanford University School of Medicine, Stanford, CA

Introduction: Identification and understanding of the cells and processes that can generate, sustain and influence the HSC niche and